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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/360,199	07/23/1999	JACK GAULDIE	GDI-1	3800

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EXAMINER	
SCHNIZER, RICHARD A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 02/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/360,199	GAULDIE ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *28 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/28/03 has been entered.

Claims 30-32 were canceled as requested. Claim 29 remains pending and is under consideration in this Office Action.

On 11/26/02 Applicant submitted a supplemental response to a non-final rejection. The response contained an expert declaration from Dr. Jack Gauldie in which protective local immunity against herpes virus-2 (HSV-2) was obtained by vaccinating a mouse with an adenoviral vector AdgB that encodes HSV gB8 protein. A final rejection was subsequently written indicating a scope of enablement for methods and compositions for delivering a nucleic acid to gastrointestinal or genitourinary cells, wherein an immune response is induced against an antigen encoded and expressed by the nucleic acid, and for a method of providing a protective immune response against HSV-2 infection. The Examiner indicated this scope of enablement in error because, while the specification discloses that adenovirus vectors can be used for vaccination against herpes viruses, it does not explicitly disclose an adenovirus vector encoding any HSV-2 antigen, or method of providing a protective immune response against HSV-2 infection, as discussed more fully below.

Drawings

The Drawings stand objected to for the reasons of record in the Notice of Draftsperson's Drawing Review (Form 948) attached to Paper No. 13.

Claim Objections

Claim 29 is objected to because a space has been inserted between the letters 'o' and 'f' in the word "of", in the penultimate line of the claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

Claim 29 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 29 was amended to require an adenoviral vector encoding an antigen derived from HSV-2, and a method of vaccinating a recipient such that onset of infection by HSV-2 is inhibited or prevented upon challenge with HSV-2. The specification as filed does not provide support for an adenoviral vector encoding an antigen derived from

HSV-2, or for methods of using it to inhibit or prevent the onset of infection by HSV-2 as claimed. The specification at paragraph 31 teaches that:

> "adenovectors have shown promise as vectors capable of immunizing against rabies and herpes viruses and more recently cancer, through DNA vaccination (Rolph, 1997)."

However, Rolph (Curr. Opin. Immunol. 9(517-524, 1997) supports only an adenoviral vector encoding a bovine herpes virus type 1 glycoprotein gD, and does not teach any HSV-2 antigen or any method of inhibiting or preventing onset of HSV-2 infection. See the entire document, especially page 518, column 1, last three paragraphs, particularly the last paragraph.

Enablement

Claim 29 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant invention requires an adenoviral vector encoding an antigen derived from HSV-2, and a method of using it to inhibit or prevent the onset of infection by HSV-2. However the specification fails to disclose any adenoviral vector encoding an HSV-2 antigen or any method of inhibiting HSV-2 infection. The specification incorporates by reference the teachings of Rolph (1997), but Rolph discloses only bovine herpes virus type 1 glycoprotein gD. See above under new matter.

While Applicant is not required to disclose that which is well known in the art, there is an obligation to disclose critical elements of the invention as well as how to use these elements. In Genentech, Inc, v Novo Nordisk A/S, the court found that when the specification omits any specific starting material required to practice an invention, or the conditions under which a process can be carried out, there is a failure to meet the enablement requirement. See 42 USPQ2d 1001.

> It is true, as Genentech argues, that a specification need not disclose what is well known in the art. See, e.g., Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research.

In this case, the adenoviral vector encoding HSV-2 antigens is a critical element required to practice the claimed method which cannot be overlooked in the course of providing an enabling disclosure, so there is a failure to meet the enablement requirement.

In the event that Applicant can show that Rolph, or some other incorporated reference, fairly discloses an adenoviral vector encoding an HSV-2 antigen and a method of inhibiting HSV-2 infection, Applicant is reminded that in any application which is to issue as a U.S. patent, essential material may not be incorporated by reference to (1) patents or applications published by foreign countries or a regional patent office, (2) non-patent publications, (3) a U.S. patent or application which itself incorporates

"essential material" by reference, or (4) a foreign application. See MPEP608.01(p), and In re Fouche, 439 F.2d 1237, 169 USPQ 429 (CCPA 1971). The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant would be required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 29 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 29 is indefinite because it recites "step (a)" and "said recipient" without antecedent basis.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Henning et al (WO 93/19660, published 10/147/93) in view of Gallichan et al (J. Infect. Dis. 168:622-629, 1993) and Cohen et al (US Patent 4,709,011, issued 11/24/1987).

This rejection is directed to the embodiment of the invention wherein adenoviruses are delivered to gastrointestinal cells.

Henning teaches a method for delivering biologically active genes to the intestinal epithelium wherein the genes are expressed. See entire document, especially abstract. The nucleic acid may be delivered as an adenovirus (see page 9, lines 11-13), and may be delivered with a mucolytic agent (see page 11, lines 25-28,. page 23, lines 1-11, and claims 61 and 62 on page 36). Henning teaches that the method may be used to induce an immune response against an antigen encoded by the nucleic acid (see page 3, lines 19-2 1).

Henning does not teach a working example of the induction of an immune response, nor does Henning teach an adenovirus encoding an HSV-2 antigen.

Gallichan teaches a method of protecting mice against infection by intravaginally administered HSV-2 by intranasal administration of an adenoviral vaccine encoding gB protein of HSV-1.

Cohen teaches that HSV-1 and HSV-2 gB and gD proteins comprise the same antigenic determinants. See column 4, lines 37-50.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the method of Henning to deliver to gastrointestinal cells an adenoviral vector encoding an HSV-2 antigen. One would have been motivated to do so with a reasonable expectation of success because Gallichan showed that mucosal immunization with adenovirus encoding HSV-1 gB provided protection against HSV-2 infection at sites distal to the site of immunization, and because Gallichan teaches that it was well known in the art that enterically delivered adenoviruses were effective as mucosal viral vectors (see page 622, column 2, lines 1-7). It would have been obvious to substitute a nucleic acid encoding the HSV-2 gB of Cohen for the HSV-1 gB of Gallichan because Cohen teaches that teaches that HSV-1 and HSV-2 gB and gD proteins comprise the same antigenic determinants. MPEP 2144.06 indicates that when it is recognized in the art that elements of an invention can be substituted, one for the other, while retaining essential function, such elements are art-recognized equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout, 675 F.2d 297, 213 USPQ 532 (CCPA 1982).

Thus the invention as a whole was prima facie obvious.

Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Henning et al (WO 93/19660, published 10/147/93) in view of Gallichan et al (J. Infect. Dis. 168:622-629, 1993) and Cohen et al (US Patent 4,709,011, issued 11/24/1987), and Wang et al (Vaccine 15(8): 821-825, 1997).

This rejection is directed to the embodiment of the invention wherein adenoviruses are delivered to genitourinary cells.

The teachings of Henning, Gallichan, and Cohen are discussed above and can be combined to render obvious methods of inhibition HSV-2 infection by delivery to gastrointestinal cells of an adenovirus encoding HSV-2 gB protein.

These references do not teach delivery to genitourinary cells.

Wang teaches a method of inducing an immune response by delivering a naked nucleic acid to genitourinary and cells in a chimpanzee. See abstract. When the method was used to deliver nucleic acids including retroviral sequences encoding HIV envelope proteins, an immune response against the envelope proteins was detected. See e.g. Fig. 2 on page 624.

In view of the fact that Gallichan shows that adenoviral vaccine delivery to mucosal surfaces distal to the site of infection can provide protection against HSV-2 infection, one of ordinary skill in the art could have delivered such a vector to the mucosa at a site of infection in a mouse (the vagina) with a reasonable expectation of success. The site of delivery is a matter of design choice which is optimized as a matter of routine by those of ordinary skill in the art. Further, one would have found motivation to deliver to the genitourinary tract because Wang shows that an expression vector-based vaccine functioned to raise an immune response when delivered to this site.

Thus the invention as a whole was prima facie obvious.

The Office wishes to make of record either one of Engler et al (US Patent 6,312,681) in which is taught a method of delivering recombinant adenoviruses to the

genitourinary tract wherein the delivery site is treated with ethanol. Specifically, Engler teaches that the "interaction of ethanol with the protective glycosaminoglycan (GAG) layer on the epithelium surface provides a mechanism for an observed increase in transgene expression. Disruption of this layer may facilitate virus-cell interaction at the surface and potentially enhance penetration into the sub mucosa." Expression of transgenes was enhanced by treatment of tissue with ethanol. See column 8, lines 1-16. this is evidence that it was routine in the art at the time of the invention to disrupt the genitourinary mucosa in order to deliver adenoviral expression vectors.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:20 AM and 3:50 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, John Leguyader, be reached at 571-272-0760. The official central fax number is 703-872-9306. Inquiries of a general nature or relating to the status of the application should be directed to the Patent Analyst Trina Turner whose telephone number is 571-272-0564.

Richard Schnizer, Ph.D.

DAVE T. NGUYEN
PRIMARY EXAMINER